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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,084	10/24/2001	Avi J. Ashkenazi	GNE.2630P1C66	4358

35489 7590 01/13/2005

HELLER EHRMAN WHITE & MCAULIFFE LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CO 94025-3506

EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,084	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	David J Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/8/2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59-65,68-70 and 74-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-65 and 74-85* is/are rejected.

7)☒ Claim(s) *68-70* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Exhibits A & B*.

DETAILED ACTION

1. Claims 1-58, 66-67 and 71-73 have been canceled.

Claims 59-65, 68-69 and 76 have been amended.

Claims 78-85 have been added.

2. Claims 59-65, 68-70 and 74-85 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This Office Action contains New Grounds of Rejections.

Objections/Rejections Withdrawn

5. The rejection of claim 76 under 35 U.S.C 101 as being drawn to non-statutory subject matter is withdrawn in view of the amendment to the claim.

6. The rejections of claims 58 and 71-73, part a, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the cancellation of the claims.

7. The rejection of claims 58 and 74-77 under 35 U.S.C. 102(b) as being anticipated by Struyk et al is withdrawn in view of Applicant's arguments and the amendments to the claims.

Response to Arguments

8. The rejection of claims 59-62 and 74 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

With respect to part a under item no. 16 of the previous Office Action (mailed 6/10/2004), the response filed 11/8/2004 has been carefully considered, but is deemed not to be persuasive. The response argues that the claims have been amended to recite an isolated nucleic acid encoding a polypeptide having at least 85-99% identity to the amino acid sequence of (a) or (b) or (c) or (d) or (e) and therefore, the phrase "wherein the nucleic acid encodes a polypeptide that is a mitogen for inner ear supporting cells" clearly refers to the isolated nucleic acids having at least 85-99% identity wherein these nucleic acids encode polypeptides that are mitogens for inner ear supporting cells. In response to this argument, it is pointed out that parts (c), (d) and (e) of claims 59-62 are drawn to nucleic acids and not amino acid sequences. Thus, as parts (c), (d) and (e) of claims 59-62 are drawn to the nucleic acid sequence of SEQ ID NO:522 or the full-length coding sequence of SEQ ID NO:522 and the preamble of the claims are drawn to variant nucleic acid sequences and fragments encoding variant polypeptides (i.e., 85-99% identity to SEQ ID NO:523). It remains unclear which of these nucleic acid sequences the phrase "wherein the nucleic acid encodes a polypeptide that is a mitogen for inner ear supporting cells" refers to.

With respect to part b under item no 16 of the previous Office Action (mailed 6/10/2004) the response filed 11/8/2004 did not address the lack of antecedent basis for

the limitation "the nucleic acid" and as discussed above it remains unclear which nucleic acid the phrase refers to and part (e) of the claims does not recite any "nucleic acid".

New Grounds of Objections/Rejections

9. Claims 59-62 are objected to as being dependent upon a cancelled claim.

Appropriate correction is required.

10. Claims 59-65 and 74-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite for reciting "The isolated nucleic acid of Claim 58 encoding a polypeptide having at least 85-99% sequence identity to:" in claims 59-62. Parts (c), (d) and (e) of the claims are drawn to nucleic acid sequences and not polypeptide sequences, thus, the claims are drawn to a polypeptide having at least 85-99% identity to the nucleic acid sequences of parts (c), (d) and (e). Are the claims drawn to nucleic acid sequences having 85-99% identity with the nucleic acid sequences of parts (c), (d) and (e) or are the claims drawn to nucleic acids which encode polypeptides having 85-99% identity with the amino acid sequences encoded by the nucleic acids of parts (c), (d) and (e) of the claims? Further, claims 63-65 are indefinite for reciting "An isolated nucleic acid comprising:" the nucleic acid of parts (c), (d) and (e) (see claim 63) and for reciting "The isolated nucleic acid of Claim 63 comprising the amino acid sequence". It is unclear what is contemplated by the

phrases as nucleic acids may encode amino acid sequences, but do not comprise amino acid sequences.

Priority

The Examiner acknowledges and agrees with applicant's assessment that patentable utility for the subject matter defined in claims 59-65, 68-70 and 74-77 is based on the proliferation of rat utricular supporting cells assay (Example 116 at page 277 of WO 99/46281), which was first disclosed in PCT/US99/05028 (WO 99/46281), filed 3/8/1999 and patentable utility for the subject matter defined in claims 74-85 is based on the chondrocyte re-differentiation assay (Example 126 at page 359) and the glucose/FFA uptake assay (Example 117 at pages 355-356 of WO 00/53756) first disclosed in PCT/US00/04341 (WO 00/53756), filed 2/18/2000. Therefore, claims 59-65, 68-70 and 74-77 are granted the priority to 3/8/1999 and claims 74-85 are granted priority to 2/18/2000.

11. Claims 59-61, 74-80 and 82-84 are rejected under 35 U.S.C. 102(b) as being anticipated by Struyk et al (The Journal of Neuroscience, 15(3):2141-2156, March 1995) as evidenced by Gil et al (Journal of Neurobiology, 51:190-204, 2002).

The claims are interpreted as being drawn to isolated nucleic acids encoding a polypeptide having 85-95% identity to the amino acid sequence of SEQ ID NO:523, optionally lacking its associated signal peptide, wherein the encoded polypeptide is a mitogen for inner ear supporting cells, induces chondrocyte re-differentiation and stimulates the uptake of glucose or FFA by adipocyte cells. The claims are also drawn

to a vector comprising the nucleic acids and a host cell comprising said vector, wherein the host cell is a CHO cell, an E.coli or a yeast cell.

Struyk et al teach a polynucleotide sequence encoding a polypeptide having 97% identity with the amino acid sequence of the polypeptide of SEQ ID NO:523 lacking its associated signal peptide, the amino acid sequence of the polypeptide encoded by the full-length coding sequence of SEQ ID NO:522, and the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209487 (see Figure 3 and the alignment attached to the back of this Office Action; Exhibit A). Struyk et al teach that the polynucleotide was isolated from a Stratgene P5 rat brain library and plasmid rescue was carried out by excision with R408 helper phage (see page 2142, right column). Thus, Struyk et al teach a vector/plasmid comprising a polynucleotide encoding a polypeptide having 97% identity with the amino acid sequence of the polypeptide of SEQ ID NO:523 lacking its associated signal peptide, the amino acid sequence of the polypeptide encoded by the full-length coding sequence of SEQ ID NO:522, and the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 209487 as well as host cells comprising said vector/plasmid. Struyk et al also teach that the polynucleotide encodes a rat neurotrimin polypeptide having 97% identity with the polypeptide of SEQ ID NO:523, lacking its associated signal peptide (i.e., full-length coding sequence) (see Figure 3 and the sequence attached to the back of this Office action; residues 29-344 of SEQ ID NO:523) and neurotrimin is a member of the immunoglobulin gene superfamily (IgSF) of

glycorylphosphatidylinositol (GPI) anchored cell adhesion molecules (see page 2141, right column and abstract). Further, Struyk et al teach that the cell adhesion molecules of the IgSF constitute a large family of proteins implicated in neural cell interactions and nerve fiber outgrowth during development (see bridging paragraph of pages 1214-1242. As evidenced by Gil et al (Journal of Neurobiology, 51:190-204, 2002) neurotrimin is a member of the IgLON family of GPI-anchored neural cell adhesion molecules (see abstract). As evidenced by the instant specification, the polynucleotide of SEQ ID NO:522, which encodes SEQ ID NO:523 (i.e., PRO337) is a newly identified member of the IgLON subfamily of the immunoglobulin superfamily and may possess neurite growth and differentiation potentiating properties (see page 179, lines 36-37). Therefore, it is the Examiner's position that Struyk et al have produced a polynucleotide, which encodes a polypeptide that is a mitogen for inner ear supporting cells, induces chondrocyte re-differentiation and stimulates the uptake of glucose or FFA by adipocyte cells. One of ordinary skill in the art would reasonably conclude that the neurotrimin polypeptide of Struyk et al also possesses the same functional properties as those of the encoded polypeptides of SEQ ID NO:523 claimed and, therefore, it appears that Struyk et al has produced a polynucleotide that encodes a polypeptide that is functionally identical to the encoded polypeptide of SEQ ID NO:523 lacking its associated signal peptide. Since the Patent and Trademark Office does not have the facilities for examining and comparing the encoded polypeptide of SEQ ID NO:523 lacking its associated signal peptide claimed with the polypeptide of Struyk et al, the burden of proof is upon the Applicant to show a distinction between the functional

characteristics of the claimed encoded polypeptide of SEQ ID NO:523 lacking its associated signal peptide and the encoded polypeptide of the prior art (Struyk et al). See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claims 74-85 are rejected under 35 U.S.C. 102(a) as being anticipated by Fukushima et al [a] (WO 99/58668, 11/18/1999) as evidenced by English equivalent Fukushima et al [b] (U.S. Patent 6,664,383 B1).

The claims are interpreted as being drawn to isolated nucleic acids encoding a polypeptide having 85-99% identity to the amino acid sequence of SEQ ID NO:523, optionally lacking its associated signal peptide, wherein the encoded polypeptide is induces chondrocyte re-differentiation and stimulates the uptake of glucose or FFA by adipocyte cells. The claims are also drawn to a vector comprising the nucleic acids and a host cell comprising said vector, wherein the host cell is a CHO cell, an E.coli or a yeast cell.

Fukushima et al [a] teach an isolated nucleic acid encoding a polypeptide identical to the polypeptide of SEQ ID NO:523 (see SEQ ID NO:1 of Fukushima et al and the alignments attached to the back of this Office Action as Exhibit B). Fukushima et al teach a vector comprising the isolated nucleic acid and host cells comprising the vector, wherein the host cells are bacterial, yeast, insect or mammalian cells as evidenced by Fukushima et al [b] (see column 3 and SEQ ID Nos:1 and 2).

Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Conclusions

14. No claim is allowed.

15. Claims 68-70 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER

Exhibit A

```
Qy        281 IlePhePheAsnValSerGluHisAspTyrGlyAsnTyrThrCysValAlaSerAsnLys 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1105 ATCTTCTTCAATGTCTCTGAACATGACTATGGGAACTACACTTGCGTGGCCTCCAACAAG 1164

Qy        301 LeuGlyHisThrAsnAlaSerIleMetLeuPheGlyProGlyAlaValSerGluValSer 320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1165 CTGGGCCACACCAATGCCAGCATCATGCTATTTGGTCCAGGCGCCGTCAGCGAGGTGAGC 1224

Qy        321 AsnGlyThrSerArgArgAlaGlyCysValTrpLeuLeuProLeuLeuValLeuHisLeu 340
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1225 AACGGCACGTCGAGGAGGGCAGGCTGCGTCTGGCTGCTGCCTCTTCTGGTCTTGCACCTG 1284

Qy        341 LeuLeuLysPhe 344
              ||||||||||||
Db       1285 CTTCTCAAATTT 1296
```

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RESULT 10
RNU16845
LOCUS       RNU16845               2040 bp    mRNA    linear   ROD 26-MAY-1995
DEFINITION  Rattus norvegicus neurotrimin mRNA, complete cds.
ACCESSION   U16845
VERSION     U16845.1  GI:755184
KEYWORDS    .
SOURCE      Rattus norvegicus (Norway rat)
  ORGANISM  Rattus norvegicus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae;
            Rattus.
REFERENCE   1  (bases 1 to 2040)
  AUTHORS   Struyk,A.P., Canoll,P.D., Wolfgang,M.J., Rosen,C.L., D'Eustachio,P.
            and Salzer,J.L.
  TITLE     Cloning of neurotrimin defines a new subfamily of differentially
            expressed neural cell adhesion molecules
  JOURNAL   J. Neurosci. 15 (3 Pt 2), 2141-2156 (1995)
  MEDLINE   95198094
   PUBMED   7891157
REFERENCE   2  (bases 1 to 2040)
  AUTHORS   Salzer,J.L.
  TITLE     Direct Submission
  JOURNAL   Submitted (02-NOV-1994) James L. Salzer, Cell Biology, NYU Medical
            Center, 550 First Avenue, New York, NY 10016, USA
FEATURES             Location/Qualifiers
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                     GRPEPTVTWRHISPKAVGFVSEDEYLEIQGITREQSGEYECSASNDVAAPVVRRVNVT
                     VNYPPYISEAKGTGVPVGQKGTLQCEASAVPSAEFQWFKDDKRLVEGKKGVKVENRPF
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                     LLVLHLLLKF"
ORIGIN

Alignment Scores:
Pred. No.:              4.73e-95        Length:         2040
Score:                  2303.70         Matches:        326
Percent Similarity:     71.22%          Conservative:   13
Best Local Similarity:  68.49%          Mismatches:     4
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DB:                     10              Gaps:           19

US-10-017-084A-523 (1-344) x RNU16845 (1-2040)
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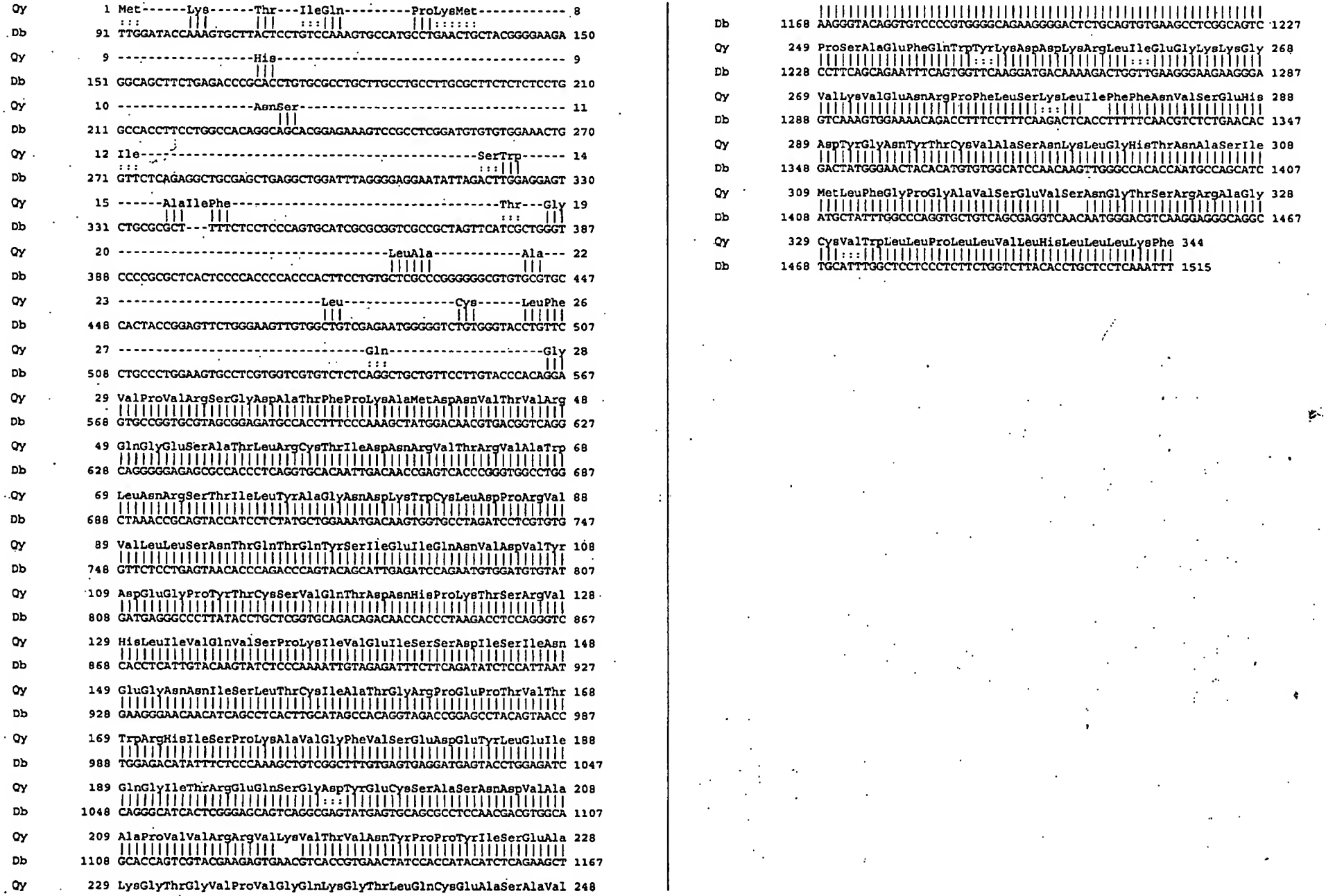
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Qy 9 ----------His---------- 9
Db 151 GGCAGCTTCTGAGACCCGCACCTGTGCGCCTGCTTGCCTGCCTTGCGCTTCTCTCTCCTG 210
Qy 10 ----------AsnSer---------- 11
Db 211 GCCACCTTCCTGGCCACAGGCAGCACGGAGAAAGTCCGCCTCGGATGTGTGTGGAAACTG 270
Qy 12 Ile----------SerTrp------ 14
Db 271 GTTCTCAGAGGCTGCGAGCTGAGGCTGGATTTAGGGGAGGAATATTAGACTTGGAGGAGT 330
Qy 15 ------AlaIlePhe----------Thr---Gly 19
Db 331 CTGCGCGCT---TTTCTCCTCCCAGTGCATCGCGCGGTCGCCGCTAGTTCATCGCTGGGT 387
Qy 20 ----------LeuAla----------Ala--- 22
Db 388 CCCCGCGCTCACTCCCCACCCCACCCACTTCCTGTGCTCGCCCGGGGGGCGTGTGCGTGC 447
Qy 23 ----------Leu----------Cys------LeuPhe 26
Db 448 CACTACCGGAGTTCTGGGAAGTTGTGGCTGTCGAGAATGGGGGTCTGTGGGTACCTGTTC 507
Qy 27 ----------Gln----------Gly 28
Db 508 CTGCCCTGGAAGTGCCTCGTGGTCGTGTCTCTCAGGCTGCTGTTCCTTGTACCCACAGGA 567
Qy 29 ValProValArgSerGlyAspAlaThrPheProLysAlaMetAspAsnValThrValArg 48
Db 568 GTGCCGGTGCGTAGCGGAGATGCCACCTTTCCCAAAGCTATGGACAACGTGACGGTCAGG 627
Qy 49 GlnGlyGluSerAlaThrLeuArgCysThrIleAspAsnArgValThrArgValAlaTrp 68
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Qy 129 HisLeuIleValGlnValSerProLysIleValGluIleSerSerAspIleSerIleAsn 148
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Db 1348 GACTATGGGAACTACACATGTGTGGCATCCAACAAGTTGGGCCACACCAATGCCAGCATC 1407
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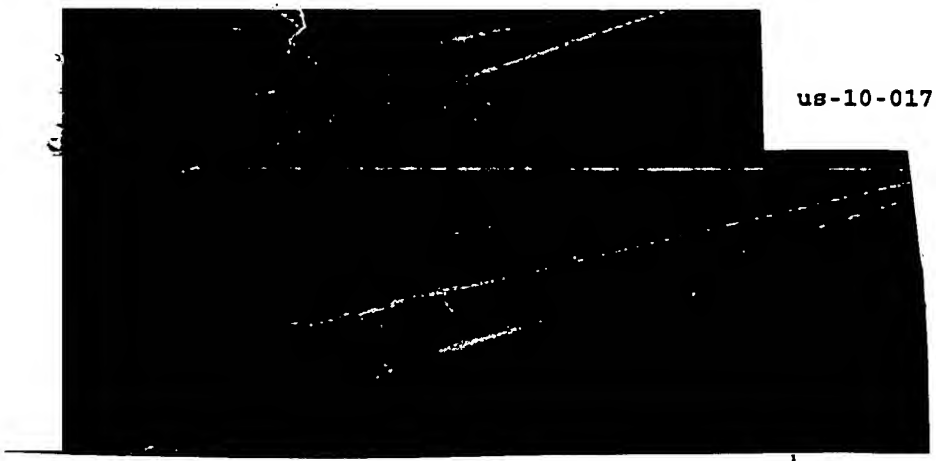

ALIGNMENTS

Exhibit B
1 of 3

RESULT 1
US-09-700-397-1
; Sequence 1, Application US/09700397
; Patent No. 6664383
; GENERAL INFORMATION:
; APPLICANT: Ono Pharmaceutical Co., Ltd.
; TITLE OF INVENTION: No. 6664383el Polypeptides, cDNA encoding the same, and use of
; FILE REFERENCE: Q61459
; CURRENT APPLICATION NUMBER: US/09/700,397
; CURRENT FILING DATE: 2001-01-05
; PRIOR APPLICATION NUMBER: JP 10-131815
; PRIOR FILING DATE: 1998-05-14
; PRIOR APPLICATION NUMBER: PCT/JP99/02485
; PRIOR FILING DATE: 1999-05-13
; NUMBER OF SEQ ID NOS: 19
; SOFTWARE: PatentIn version 3.0
; SEQ ID NO 1
; LENGTH: 1032
; TYPE: DNA
; ORGANISM: Homo sapiens
US-09-700-397-1

Alignment Scores:

Pred. No.:	9.88e-47	Length:	1032
Score:	2408.00	Matches:	344
Percent Similarity:	100.00%	Conservative:	0
Best Local Similarity:	100.00%	Mismatches:	0
Query Match:	100.00%	Indels:	0
DB:	4	Gaps:	0

US-10-017-084A-523 (1-344) x US-09-700-397-1 (1-1032)

```
Qy          1 MetLysThrIleGlnProLysMetHisAsnSerIleSerTrpAlaIlePheThrGlyLeu 20
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 ATGAAAACCATCCAGCCAAAAATGCACAATTCTATCTCTTGGGCAATCTTCACGGGGCTG 60

Qy         21 AlaAlaLeuCysLeuPheGlnGlyValProValArgSerGlyAspAlaThrPheProLys 40
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GCTGCTCTGTGTCTCTTCCAAGGAGTGCCCGTGCGCAGCGGAGATGCCACCTTCCCCAAA 120

Qy         41 AlaMetAspAsnValThrValArgGlnGlyGluSerAlaThrLeuArgCysThrIleAsp 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 GCTATGGACAACGTGACGGTCCGGCAGGGGGAGAGCGCCACCCTCAGGTGCACTATTGAC 180

Qy         61 AsnArgValThrArgValAlaTrpLeuAsnArgSerThrIleLeuTyrAlaGlyAsnAsp 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 AACCGGGTCACCCGGGTGGCCTGGCTAAACCGCAGCACCATCCTCTATGCTGGGAATGAC 240

Qy         81 LysTrpCysLeuAspProArgValValLeuLeuSerAsnThrGlnThrGlnTyrSerIle 100
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 AAGTGGTGCCTGGATCCTCGCGTGGTCCTTCTGAGCAACACCCAAACGCAGTACAGCATC 300

Qy        101 GluIleGlnAsnValAspValTyrAspGluGlyProTyrThrCysSerValGlnThrAsp 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 GAGATCCAGAACGTGGATGTGTATGACGAGGGCCCTTACACCTGCTCGGTGCAGACAGAC 360

Qy        121 AsnHisProLysThrSerArgValHisLeuIleValGlnValSerProLysIleValGlu 140
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Db        361 AACCACCCAAAGACCTCTAGGGTCCACCTCATTGTGCAAGTATCTCCCAAAATTGTAGAG 420

Qy        141 IleSerSerAspIleSerIleAsnGluGlyAsnAsnIleSerLeuThrCysIleAlaThr 160
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 ATTTCTTCAGATATCTCCATTAATGAAGGGAACAATATTAGCCTCACCTGCATAGCAACT 480

Qy        161 GlyArgProGluProThrValThrTrpArgHisIleSerProLysAlaValGlyPheVal 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 GGTAGACCAGAGCCTACGGTTACTTGGAGACACATCTCTCCCAAAGCGGTTGGCTTTGTG 540

Qy        181 SerGluAspGluTyrLeuGluIleGlnGlyIleThrArgGluGlnSerGlyAspTyrGlu 200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 AGTGAAGACGAATACTTGGAAATTCAGGGCATCACCCGGGAGCAGTCAGGGGACTACGAG 600

Qy        201 CysSerAlaSerAsnAspValAlaAlaProValValArgArgValLysValThrValAsn 220
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 TGCAGTGCCTCCAATGACGTGGCCGCGCCCGTGGTACGGAGAGTAAAGGTCACCGTGAAC 660

Qy        221 TyrProProTyrIleSerGluAlaLysGlyThrGlyValProValGlyGlnLysGlyThr 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 TATCCACCATACATTTCAGAAGCCAAGGGTACAGGTGTCCCCGTGGGACAAAAGGGGACA 720

Qy        241 LeuGlnCysGluAlaSerAlaValProSerAlaGluPheGlnTrpTyrLysAspAspLys 260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 CTGCAGTGTGAAGCCTCAGCAGTCCCCTCAGCAGAATTCCAGTGGTACAAGGATGACAAA 780

Qy        261 ArgLeuIleGluGlyLysLysGlyValLysValGluAsnArgProPheLeuSerLysLeu 280
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Db        781 AGACTGATTGAAGGAAAGAAAGGGGTGAAAGTGGAAAACAGACCTTTCCTCTCAAAACTC 840

Qy        281 IlePhePheAsnValSerGluHisAspTyrGlyAsnTyrThrCysValAlaSerAsnLys 300
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Db        841 ATCTTCTTCAATGTCTCTGAACATGACTATGGGAACTACACTTGCGTGGCCTCCAACAAG 900

Qy        301 LeuGlyHisThrAsnAlaSerIleMetLeuPheGlyProGlyAlaValSerGluValSer 320
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Db        901 CTGGGCCACACCAATGCCAGCATCATGCTATTTGGTCCAGGCGCCGTCAGCGAGGTGAGC 960

Qy        321 AsnGlyThrSerArgArgAlaGlyCysValTrpLeuLeuProLeuLeuValLeuHisLeu 340
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Db        961 AACGGCACGTCGAGGAGGGCAGGCTGCGTCTGGCTGCTGCCTCTTCTGGTCTTGCACCTG 1020

Qy        341 LeuLeuLysPhe 344
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Db       1021 CTTCTCAAATTT 1032
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RESULT 2
US-09-700-397-2
; Sequence 2, Application US/09700397
; Patent No. 6664383
; GENERAL INFORMATION:
; APPLICANT: Ono Pharmaceutical Co., Ltd.
; TITLE OF INVENTION: No. 6664383el Polypeptides, cDNA encoding the same, and use of
; FILE REFERENCE: Q61459
; CURRENT APPLICATION NUMBER: US/09/700,397
; CURRENT FILING DATE: 2001-01-05
; PRIOR APPLICATION NUMBER: JP 10-131815
; PRIOR FILING DATE: 1998-05-14
; PRIOR APPLICATION NUMBER: PCT/JP99/02485
; PRIOR FILING DATE: 1999-05-13
; NUMBER OF SEQ ID NOS: 19
; SOFTWARE: PatentIn version 3.0
; SEQ ID NO 2
; LENGTH: 1693
; TYPE: DNA
; ORGANISM: Homo sapiens
; FEATURE:
; NAME/KEY: misc_feature
; OTHER INFORMATION: Clone OC001 derived from human brain

Exhibit B
2 of 3

; NAME/KEY: CDS
; LOCATION: (130)..(1161)
; NAME/KEY: sig_peptide
; LOCATION: (130)..(213)
; NAME/KEY: mat_peptide
; LOCATION: (214)..()
US-09-700-397-2

Alignment Scores:

Pred. No.:	8.18e-46	Length:	1693
Score:	2408.00	Matches:	344
Percent Similarity:	100.00%	Conservative:	0
Best Local Similarity:	100.00%	Mismatches:	0
Query Match:	100.00%	Indels:	0
DB:	4	Gaps:	0

US-10-017-084A-523 (1-344) x US-09-700-397-2 (1-1693)

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Db        130 ATGAAAACCATCCAGCCAAAAATGCACAATTCTATCTCTTGGGCAATCTTCACGGGGCTG 189

Qy         21 AlaAlaLeuCysLeuPheGlnGlyValProValArgSerGlyAspAlaThrPheProLys 40
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Db        190 GCTGCTCTGTGTCTCTTCCAAGGAGTGCCCGTGCGCAGCGGAGATGCCACCTTCCCCAAA 249

Qy         41 AlaMetAspAsnValThrValArgGlnGlyGluSerAlaThrLeuArgCysThrIleAsp 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        250 GCTATGGACAACGTGACGGTCCGGCAGGGGGAGAGCGCCACCCTCAGGTGCACTATTGAC 309

Qy         61 AsnArgValThrArgValAlaTrpLeuAsnArgSerThrIleLeuTyrAlaGlyAsnAsp 80
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        310 AACCGGGTCACCCGGGTGGCCTGGCTAAACCGCAGCACCATCCTCTATGCTGGGAATGAC 369

Qy         81 LysTrpCysLeuAspProArgValValLeuLeuSerAsnThrGlnThrGlnTyrSerIle 100
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Db        370 AAGTGGTGCCTGGATCCTCGCGTGGTCCTTCTGAGCAACACCCAAACGCAGTACAGCATC 429

Qy        101 GluIleGlnAsnValAspValTyrAspGluGlyProTyrThrCysSerValGlnThrAsp 120
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Db        430 GAGATCCAGAACGTGGATGTGTATGACGAGGGCCCTTACACCTGCTCGGTGCAGACAGAC 489

Qy        121 AsnHisProLysThrSerArgValHisLeuIleValGlnValSerProLysIleValGlu 140
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Db        490 AACCACCCAAAGACCTCTAGGGTCCACCTCATTGTGCAAGTATCTCCCAAAATTGTAGAG 549

Qy        141 IleSerSerAspIleSerIleAsnGluGlyAsnAsnIleSerLeuThrCysIleAlaThr 160
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Db        550 ATTTCTTCAGATATCTCCATTAATGAAGGGAACAATATTAGCCTCACCTGCATAGCAACT 609

Qy        161 GlyArgProGluProThrValThrTrpArgHisIleSerProLysAlaValGlyPheVal 180
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Db        610 GGTAGACCAGAGCCTACGGTTACTTGGAGACACATCTCTCCCAAAGCGGTTGGCTTTGTG 669

Qy        181 SerGluAspGluTyrLeuGluIleGlnGlyIleThrArgGluGlnSerGlyAspTyrGlu 200
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Db        670 AGTGAAGACGAATACTTGGAAATTCAGGGCATCACCCGGGAGCAGTCAGGGGACTACGAG 729

Qy        201 CysSerAlaSerAsnAspValAlaAlaProValValArgArgValLysValThrValAsn 220
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Db        730 TGCAGTGCCTCCAATGACGTGGCCGCGCCCGTGGTACGGAGAGTAAAGGTCACCGTGAAC 789

Qy        221 TyrProProTyrIleSerGluAlaLysGlyThrGlyValProValGlyGlnLysGlyThr 240
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Db        790 TATCCACCATACATTTCAGAAGCCAAGGGTACAGGTGTCCCCGTGGGACAAAAGGGGACA 849

Qy        241 LeuGlnCysGluAlaSerAlaValProSerAlaGluPheGlnTrpTyrLysAspAspLys 260
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Db        850 CTGCAGTGTGAAGCCTCAGCAGTCCCCTCAGCAGAATTCCAGTGGTACAAGGATGACAAA 909

Qy        261 ArgLeuIleGluGlyLysLysGlyValLysValGluAsnArgProPheLeuSerLysLeu 280
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Db        910 AGACTGATTGAAGGAAAGAAAGGGGTGAAAGTGGAAAACAGACCTTTCCTCTCAAAACTC 969

Qy        281 IlePhePheAsnValSerGluHisAspTyrGlyAsnTyrThrCysValAlaSerAsnLys 300
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Db        970 ATCTTCTTCAATGTCTCTGAACATGACTATGGGAACTACACTTGCGTGGCCTCCAACAAG 1029

Qy        301 LeuGlyHisThrAsnAlaSerIleMetLeuPheGlyProGlyAlaValSerGluValSer 320
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Db       1030 CTGGGCCACACCAATGCCAGCATCATGCTATTTGGTCCAGGCGCCGTCAGCGAGGTGAGC 1089

Qy        321 AsnGlyThrSerArgArgAlaGlyCysValTrpLeuLeuProLeuLeuValLeuHisLeu 340
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Db       1090 AACGGCACGTCGAGGAGGGCAGGCTGCGTCTGGCTGCTGCCTCTTCTGGTCTTGCACCTG 1149

Qy        341 LeuLeuLysPhe 344
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Db       1150 CTTCTCAAATTT 1161
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RESULT 3
US-09-700-397-5
; Sequence 5, Application US/09700397
; Patent No. 6664383
; GENERAL INFORMATION:
; APPLICANT: Ono Pharmaceutical Co., Ltd.
; TITLE OF INVENTION: No. 6664383el Polypeptides, cDNA encoding the same, and use of
; FILE REFERENCE: Q61459
; CURRENT APPLICATION NUMBER: US/09/700,397
; CURRENT FILING DATE: 2001-01-05
; PRIOR APPLICATION NUMBER: JP 10-131815
; PRIOR FILING DATE: 1998-05-14
; PRIOR APPLICATION NUMBER: PCT/JP99/02485
; PRIOR FILING DATE: 1999-05-13
; NUMBER OF SEQ ID NOS: 19
; SOFTWARE: PatentIn version 3.0
; SEQ ID NO 5
; LENGTH: 939
; TYPE: DNA
; ORGANISM: Homo sapiens
US-09-700-397-5

Alignment Scores:

Pred. No.:	2.33e-41	Length:	939
Score:	2185.00	Matches:	313
Percent Similarity:	100.00%	Conservative:	0
Best Local Similarity:	100.00%	Mismatches:	0
Query Match:	90.74%	Indels:	0
DB:	4	Gaps:	0

US-10-017-084A-523 (1-344) x US-09-700-397-5 (1-939)

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Qy         52 SerAlaThrLeuArgCysThrIleAspAsnArgValThrArgValAlaTrpLeuAsnArg 71
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 AGCGCCACCCTCAGGTGCACTATTGACAACCGGGTCACCCGGGTGGCCTGGCTAAACCGC 120

Qy         72 SerThrIleLeuTyrAlaGlyAsnAspLysTrpCysLeuAspProArgValValLeuLeu 91
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 AGCACCATCCTCTATGCTGGGAATGACAAGTGGTGCCTGGATCCTCGCGTGGTCCTTCTG 180

Qy         92 SerAsnThrGlnThrGlnTyrSerIleGluIleGlnAsnValAspValTyrAspGluGly 111
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Db        181 AGCAACACCCAAACGCAGTACAGCATCGAGATCCAGAACGTGGATGTGTATGACGAGGGC 240

Qy        112 ProTyrThrCysSerValGlnThrAspAsnHisProLysThrSerArgValHisLeuIle 131
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Db        241 CCTTACACCTGCTCGGTGCAGACAGACAACCACCCAAAGACCTCTAGGGTCCACCTCATT 300

Qy        132 ValGlnValSerProLysIleValGluIleSerSerAspIleSerIleAsnGluGlyAsn 151
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Db        301 GTGCAAGTATCTCCCAAAATTGTAGAGATTTCTTCAGATATCTCCATTAATGAAGGGAAC 360
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Exhibit B
3 of 3

ALIGNMENTS

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RESULT 1
US-09-700-397-2
; Sequence 2, Application US/09700397
; Patent No. 6664383
; GENERAL INFORMATION:
;  APPLICANT:  Ono Pharmaceutical Co., Ltd.
;  TITLE OF INVENTION:   No. 6664383el Polypeptides, cDNA encoding the same, and use of
;  FILE REFERENCE:   Q61459
;  CURRENT APPLICATION NUMBER: US/09/700,397
;  CURRENT FILING DATE:  2001-01-05
;  PRIOR APPLICATION NUMBER:   JP 10-131815
;  PRIOR FILING DATE:   1998-05-14
;  PRIOR APPLICATION NUMBER:   PCT/JP99/02485
;  PRIOR FILING DATE:   1999-05-13
;  NUMBER OF SEQ ID NOS:   19
;  SOFTWARE:   PatentIn version 3.0
; SEQ ID NO 2
;   LENGTH: 1693
;   TYPE: DNA
;   ORGANISM: Homo sapiens
;   FEATURE:
;   NAME/KEY: misc_feature
;   OTHER INFORMATION: Clone OC001 derived from human brain
;   NAME/KEY: CDS
;   LOCATION: (130)..(1161)
;   NAME/KEY: sig_peptide
;   LOCATION: (130)..(213)
;   NAME/KEY: mat_peptide
;   LOCATION: (214)..()
US-09-700-397-2

  Query Match           100.0%;  Score 1035;  DB 4;  Length 1693;
  Best Local Similarity  100.0%;  Pred. No. 9.8e-11;
  Matches 1035;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

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Db        130 ATGAAAACCATCCAGCCAAAAATGCACAATTCTATCTCTTGGGCAATCTTCACGGGGCTG 189

Qy         61 GCTGCTCTGTGTCTCTTCCAAGGAGTGCCCGTGCGCAGCGGAGATGCCACCTTCCCCAAA 120
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Db        190 GCTGCTCTGTGTCTCTTCCAAGGAGTGCCCGTGCGCAGCGGAGATGCCACCTTCCCCAAA 249

Qy        121 GCTATGGACAACGTGACGGTCCGGCAGGGGGAGAGCGCCACCCTCAGGTGCACTATTGAC 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        250 GCTATGGACAACGTGACGGTCCGGCAGGGGGAGAGCGCCACCCTCAGGTGCACTATTGAC 309

Qy        181 AACCGGGTCACCCGGGTGGCCTGGCTAAACCGCAGCACCATCCTCTATGCTGGGAATGAC 240
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Db        310 AACCGGGTCACCCGGGTGGCCTGGCTAAACCGCAGCACCATCCTCTATGCTGGGAATGAC 369

Qy        241 AAGTGGTGCCTGGATCCTCGCGTGGTCCTTCTGAGCAACACCCAAACGCAGTACAGCATC 300
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Qy        301 GAGATCCAGAACGTGGATGTGTATGACGAGGGCCCTTACACCTGCTCGGTGCAGACAGAC 360
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Db        430 GAGATCCAGAACGTGGATGTGTATGACGAGGGCCCTTACACCTGCTCGGTGCAGACAGAC 489

Qy        361 AACCACCCAAAGACCTCTAGGGTCCACCTCATTGTGCAAGTATCTCCCAAAATTGTAGAG 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        490 AACCACCCAAAGACCTCTAGGGTCCACCTCATTGTGCAAGTATCTCCCAAAATTGTAGAG 549

Qy        421 ATTTCTTCAGATATCTCCATTAATGAAGGGAACAATATTAGCCTCACCTGCATAGCAACT 480
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Db        550 ATTTCTTCAGATATCTCCATTAATGAAGGGAACAATATTAGCCTCACCTGCATAGCAACT 609

Qy        481 GGTAGACCAGAGCCTACGGTTACTTGGAGACACATCTCTCCCAAAGCGGTTGGCTTTGTG 540
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Db        610 GGTAGACCAGAGCCTACGGTTACTTGGAGACACATCTCTCCCAAAGCGGTTGGCTTTGTG 669

Qy        541 AGTGAAGACGAATACTTGGAAATTCAGGGCATCACCCGGGAGCAGTCAGGGGACTACGAG 600
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Db        670 AGTGAAGACGAATACTTGGAAATTCAGGGCATCACCCGGGAGCAGTCAGGGGACTACGAG 729

Qy        601 TGCAGTGCCTCCAATGACGTGGCCGCGCCCGTGGTACGGAGAGTAAAGGTCACCGTGAAC 660
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Db        730 TGCAGTGCCTCCAATGACGTGGCCGCGCCCGTGGTACGGAGAGTAAAGGTCACCGTGAAC 789

Qy        661 TATCCACCATACATTTCAGAAGCCAAGGGTACAGGTGTCCCCGTGGGACAAAAGGGGACA 720
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Db        790 TATCCACCATACATTTCAGAAGCCAAGGGTACAGGTGTCCCCGTGGGACAAAAGGGGACA 849

Qy        721 CTGCAGTGTGAAGCCTCAGCAGTCCCCTCAGCAGAATTCCAGTGGTACAAGGATGACAAA 780
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Db        850 CTGCAGTGTGAAGCCTCAGCAGTCCCCTCAGCAGAATTCCAGTGGTACAAGGATGACAAA 909

Qy        781 AGACTGATTGAAGGAAAGAAAGGGGTGAAAGTGGAAAACAGACCTTTCCTCTCAAAACTC 840
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Db        910 AGACTGATTGAAGGAAAGAAAGGGGTGAAAGTGGAAAACAGACCTTTCCTCTCAAAACTC 969

Qy        841 ATCTTCTTCAATGTCTCTGAACATGACTATGGGAACTACACTTGCGTGGCCTCCAACAAG 900
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Db        970 ATCTTCTTCAATGTCTCTGAACATGACTATGGGAACTACACTTGCGTGGCCTCCAACAAG 1029

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Db       1030 CTGGGCCACACCAATGCCAGCATCATGCTATTTGGTCCAGGCGCCGTCAGCGAGGTGAGC 1089

Qy        961 AACGGCACGTCGAGGAGGGCAGGCTGCGTCTGGCTGCTGCCTCTTCTGGTCTTGCACCTG 1020
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Qy       1021 CTTCTCAAATTTTGA 1035
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Db       1150 CTTCTCAAATTTTGA 1164
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RESULT 2
US-09-700-397-1
; Sequence 1, Application US/09700397
; Patent No. 6664383
; GENERAL INFORMATION:
;  APPLICANT:  Ono Pharmaceutical Co., Ltd.
;  TITLE OF INVENTION:   No. 6664383el Polypeptides, cDNA encoding the same, and use of
;  FILE REFERENCE:   Q61459
;  CURRENT APPLICATION NUMBER: US/09/700,397
;  CURRENT FILING DATE:  2001-01-05
;  PRIOR APPLICATION NUMBER:   JP 10-131815
;  PRIOR FILING DATE:   1998-05-14
;  PRIOR APPLICATION NUMBER:   PCT/JP99/02485
;  PRIOR FILING DATE:   1999-05-13
;  NUMBER OF SEQ ID NOS:   19
;  SOFTWARE:   PatentIn version 3.0
; SEQ ID NO 1
;   LENGTH: 1032
;   TYPE: DNA
;   ORGANISM: Homo sapiens
US-09-700-397-1

  Query Match           99.7%;  Score 1032;  DB 4;  Length 1032;
  Best Local Similarity  100.0%;  Pred. No. 4.6e-11;
  Matches 1032;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

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Qy         61 GCTGCTCTGTGTCTCTTCCAAGGAGTGCCCGTGCGCAGCGGAGATGCCACCTTCCCCAAA 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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